ABSTRACT

**Objective:** Seborrheic dermatitis is a common relapsing inflammatory skin condition occurring in approximately 3 to 5 percent of the general population. Current available therapies control, but do not cure seborrhea. The study's objective was to determine the safety and efficacy of a barrier-based, nonsteroidal cream incorporating herbal extracts as a treatment for facial seborrheic dermatitis. **Design:** Interventional, open label, safety/efficacy study. **Setting:** At the baseline visit, the investigator selected a target area on the face. The target area was evaluated for Investigator Static Global Assessment, desquamation (scaling), induration (inflammation), and erythema (redness) as well as self-assessed pruritus. **Participants:** Thirty-two subjects with seborrheic dermatitis were enrolled in the study. **Measurements:** Subjects were instructed to use the study medication twice a day, morning and evening, for a consecutive period of 42 days. In addition to the baseline visit (Day 0), subjects visited the clinic for two follow-up visits at Days 14 and 28 and for a final visit at Day 42. At each visit, all

[Abstract continued on next page]

ORIGINAL RESEARCH

# Treatment of Seborrheic Dermatitis Using a Novel Herbal-based Cream

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Seborrheic dermatitis (SD) is a common relapsing inflammatory skin condition occurring in approximately 3 to 5 percent of the general population, with a worldwide distribution. SD affects newborns, infants, and adults; occurs in all races; and severity is higher in males than in females. Up to 70 percent of infants in the first three months of life may develop the condition. The prevalence of SD is increasing to 30 to 83 percent in human immunodeficiency virus (HIV)-positive and acquired immunodeficiency syndrome (AIDS) patients. SD is related to cradle cap or diaper rash. It is commonly worsened by changes in environment humidity, changes in seasons, trauma, or emotional stress.[1,2] Symptoms of SD include excessive sebum production (hyperseborrhea), erythematous plaques with scales, and frequent pruritus.[3,4]

Available topical therapies temporarily control the symptoms, but do not cure the condition.[5,6] Treatment for mild-to-moderate cases include antimycotic agents[7] (e.g.,

**Disclosure:** Dr. Barak-Shinar is an employee of Kamedis Ltd., the manufacturer of Seborrheamedis Face Cream and the sponsor of this study. Dr. del Río is the Principle Investigator of the Seborrheamedis Face Cream clinical trial. Dr. Green serves on the medical advisory board for Kamedis. The study was conducted in accordance with the Declaration of Helsinki. This study was wholly funded by Kamedis Ltd.

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[Abstract continued]

parameters were evaluated. **Results:** A reduction in all parameters evaluated was seen at almost all timepoints, improving more from one timepoint to the next during the study period. In addition, the patients expressed a high degree of satisfaction with the treatment. No adverse events were reported during this study. **Conclusion:** The study showed that after six weeks of treatment, the face cream provided improvement in Investigator Static Global Assessment, pruritus, desquamation, induration, and erythema. **ClinicalTrials.gov Identifier:** NCT02656368 (https://clinicaltrials.gov/ct2/show/NCT02656368?term=Kamedis&rank=2)

*J Clin Aesthet Dermatol.* 2017;10(4):17–23.

ketoconazole, bifonazole, and ciclopirox); zinc pyrithione; lithium salts and coal tars in shampoos; and selenium sulfide in shampoos, creams, and foams.[2]

Although the pathogenesis of seborrheic dermatitis has not been completely elucidated, there appears to be a strong association with yeasts of the genus *Malassezia*.[7–10] *Malassezia* has been found on affected sites, and reduction of yeast populations by treatment with antifungals is effective in providing relief for seborrheic dermatitis.[11] However, the pathogen's (*Malassezia*) resistance to antifungal agents has also been documented.[6,7]

Seborrhea can also be treated with low or medium potency topical corticosteroids or calcineurin inhibitors (e.g., tacrolimus and pimecrolimus). These immunomodulatory agents are highly effective as anti-inflammatory agents, but long-term continuous use should be avoided because of their risk of causing addiction and steroid rosacea.[8] In very severe cases, ultraviolet B (UVB) phototherapy is often considered.[11]

Seborrheamedis Face Cream (Kamedis, Israel) is a barrier-based, nonsteroidal cream incorporated with herbal extracts designed to manage the clinical manifestations and symptoms of facial seborrheic dermatitis, such as erythema, scaling, and pruritus. The aim of this study was to determine the safety and efficacy of this face cream applied twice daily for 42 days in the treatment of SD.

## METHODS

Thirty-two male and female subjects over the age of 18 were enrolled in a single-center, prospective, open-label, institutional review board (IRB)-approved, six-week study. All subjects had mild Investigator Static Global Assessment (ISGA = 2) to moderate (ISGA = 3) facial seborrheic dermatitis.

At the baseline visit, the investigator selected a target area on the face. The target area was evaluated for desquamation (scaling), induration (inflammation), and erythema (redness) using a 5-point scale: 0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe. The target area was photographed. In addition, the investigator assessed the extent of overall facial lesions using an ISGA based on a 6-point scale: 0=clear (no inflammatory signs of SD), 1=almost clear (just perceptible erythema and just perceptible papulation/induration), 2=mild (mild erythema and mild papulation/induration), 3=moderate (moderate erythema and moderate papulation/induration), 4=severe (severe erythema and severe papulation/induration), 5=very severe (very severe erythema and very severe papulation/induration with oozing/crusting). The ISGA provides the overall evaluation of the physician, taking into consideration all condition symptoms. Using a 6-point scale enables a standard definition per each scale, which assists in converting the data into an effective and efficient clinical report. The subject evaluated his/her pruritus over the past 24 hours using a 5-point scale: 0=no itching, 1=minimal and rare itching, 2=mild itching, (subject is aware of the itching only when relaxed), 3=moderate itching (subject is often aware of the itching, which

occasionally disturbs sleep), and 4=severe and constant itching.

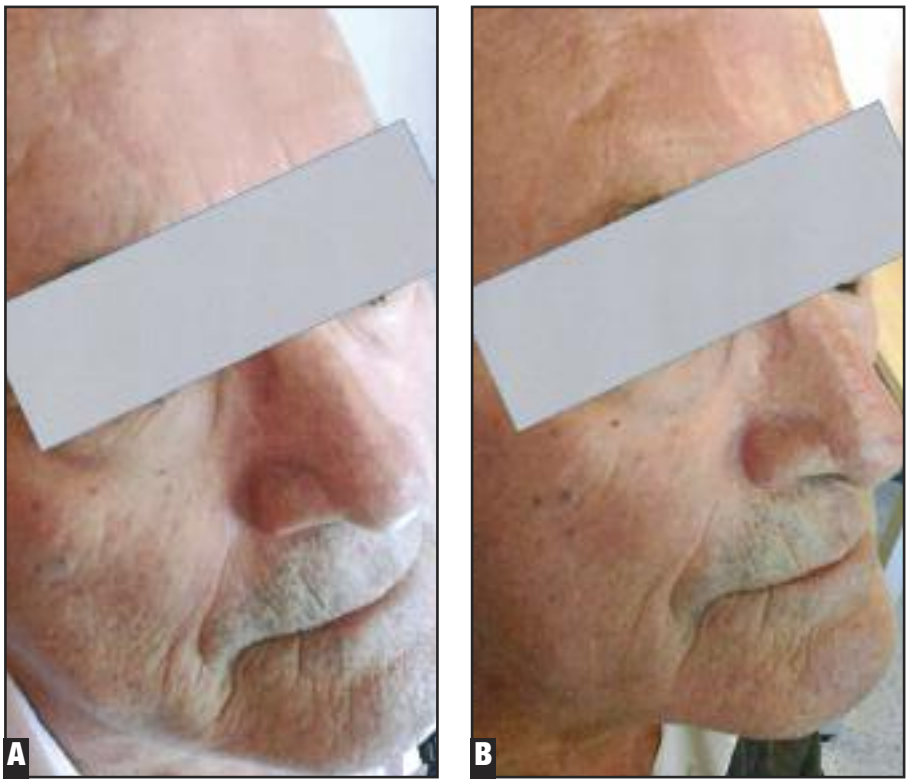
Subjects were instructed to use the study face cream twice a day, morning and evening, for a consecutive period of 42 days. In addition to the baseline visit (Day 0), subjects visited the clinic for two follow-up visits at Days 14 and 28 and for a final visit at Day 42. A flexibility of ±2 days was allowed. In case of an adverse event, the subject was asked to immediately contact the clinic and to come to an unscheduled visit if needed.

At each of the two follow-up visits and at the final visit, the investigator evaluated the overall severity of seborrhea (ISGA) and the target area's desquamation, induration, and erythema. At each visit, the subjects assessed their pruritus over the past 24 hours.

At the final visit, the subject completed a product assessment questionnaire. The questionnaire included several questions about satisfaction attributes, using a 5-point scale: -2=very unsatisfied, -1=unsatisfied, 0=neutral, +1=satisfied, +2=very satisfied. Attributes included overall satisfaction, speed of results, ease of use, ease of spread, comfort under makeup, feel on the skin (-2=very greasy, +2=very moisturizing), speed of absorption, texture, color, and odor.

**Table 1. Patient demographic characteristics**

| CHARACTERISTICS | VALUE |
|---|---|
| Men | 20 (77%) |
| Women | 6 (23%) |
| Age range (years) | 25–85 |
| Mean Age (years) | 61.1 (deviation 13.4) |




**Figures 1A and 1B.** Clinical appearance of patient with sebhorrheic dermatits (A) before and (B) after 6 weeks of treatment with a novel herbal-based cream

## RESULTS

A total of 32 patients were recruited to the study. Six patients left the study due to personal reasons not connected to the study itself, leaving 26 patients who completed the study (Table 1).

Results from each visit were compared with those from baseline using the Nonparametric Dunn Test. Analysis results showed statistically significant differences (reduction) between all tested pairs when compared to baseline (parameters and visit considering an alpha level of 5% in the probability distribution plot), which supports the hypothesis that symptoms improve with each visit.

In general, all evaluated parameters at all timepoints showed significant clinical improvement when compared to baseline. Only desquamation between Weeks 4 and 6 did not show a significant improvement from Week 4 to Week 6, even though each of these timepoints

**Table 2. Improvement achieved in the evaluated parameter: ISGA, desquamation, induration, and erythema on Weeks 2, 4, and 6**

| DURATION (NUMBER OF WEEKS) | ISGA IMPROVEMENT (%) | DESQUAMATION IMPROVEMENT (%) | INDURATION IMPROVEMENT (%) | ERYTHEMA IMPROVEMENT (%) |
|---|---|---|---|---|
| 2 | 57.7 | 61.5 | 82.7 | 53.8 |
| 4 | 69.9 | 85.3 | 89.7 | 69.2 |
| 6 | 76.3 | 80.1 | 92.9 | 77.6 |

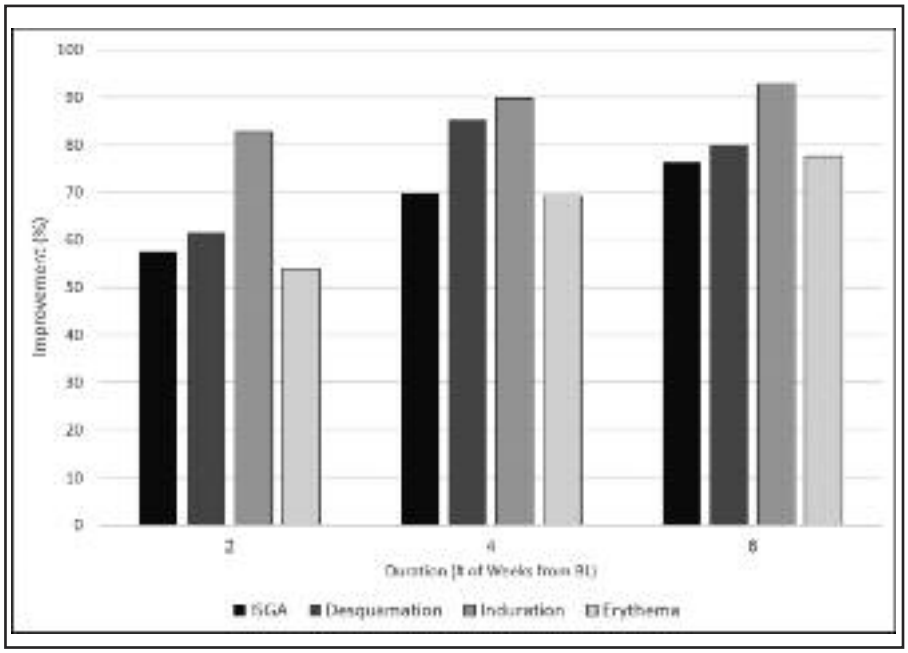



**Figure 2.** Average treatment score versus duration (weeks)

significantly improved from baseline.

In addition, clear improvement was visually evident (Figure 1). Specifically, ISGA improved 76 percent after six weeks of treatment with the product ($p<0.05$ compared to baseline [BL]). The mean score changed from 2.35 at baseline to 0.54 after six weeks. The largest percent improvement in all parameters occurred between baseline and Week 2, suggesting a fast onset of action.

Average desquamation was improved by 85 percent following four weeks of treatment ($p<0.05$ compared to BL), while the mean score changed from 1.76 at baseline to 0.38 after six weeks. Average improvement in induration reached 92.9 percent after six weeks of product treatment ($p<0.05$ compared to BL). The mean scores changed from 1.69 at baseline to 0.15 after six weeks. Average improvement in erythema reached 77.6 percent after six weeks of product treatment ($p<0.05$ compared to BL). Mean scores changed from 2.42 at baseline to 0.50 after six weeks. Average improvement of pruritus reached 94.9 percent following six weeks of treatment, based on the subject statements ($p<0.05$ compared to BL) and the mean scores changed from 2.03 at baseline to 0.15 after six weeks (Tables 2 and 3; Figures 2 and 3, respectively). As can be seen from the following figures, the evaluated parameters not only maintained their improvement, but also continued to show additional improvement until the end of the six-week study.

When asked how they liked the product, 76 percent of the subjects liked the product extremely well; 24 percent liked it really well; and 0 percent somewhat liked it, neither liked nor disliked it, or did not like the product (Table 4 and Figure 4, respectively).

When asked how satisfied they were with the speed of the improvement provided by the product, 65 percent responded very satisfied; 35 percent moderately satisfied; and 0 percent satisfied, moderately satisfied, or very

unsatisfied (Table 5 and Figure 5, respectively).

Results regarding the characteristics of the product including comfort under makeup, feel on the skin, speed of absorption, texture, color, and odor yielded a very good satisfaction rate. No adverse experiences or events occurred during the course of the trial.

**Table 3. Average pruritus self-evaluation improvement on Weeks 2, 4, and 6**

| DURATION (NUMBER OF WEEKS) | PRURITUS IMPROVEMENT (%) |
|---|---|
| 2 | 80.8 |
| 4 | 88.5 |
| 6 | 94.9 |

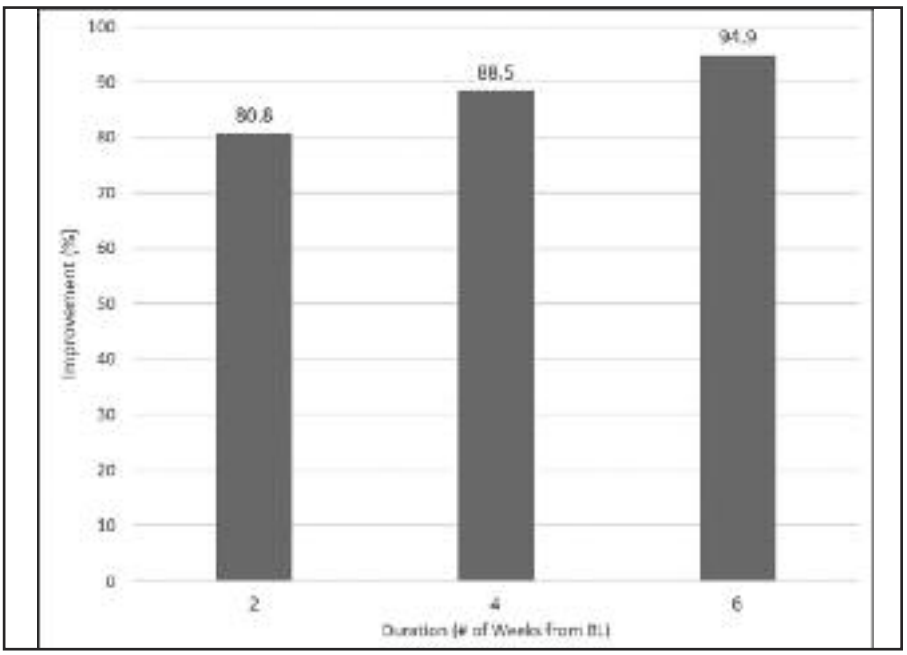



**Figure 3.** Average pruritus self-evaluation improvement (percentage compared to BL) versus duration (weeks from BL)

## DISCUSSION

In the results presented here, treatment with the herbal-based face cream significantly improved all evaluated parameters of seborrheic dermatitis when compared to baseline while presenting no safety concerns.

In previous studies concerning treatment of SD, there is a lack of standard agreed criteria for treatment outcome assessment. Variables used to assess outcome have included pruritus, desquamation, induration, erythema, and ISGA.[12–19] This investigation used all these criteria as well as patient self-assessment questionnaires to obtain a more complete picture of the efficacy and safety of the cream. In addition, a vehicle-controlled study would be a further step in better demonstrating the efficacy of the study medication. This design will be added to future investigations.

In today's world there is often an increasing demand for alternative[17] and herbal/botanical-based treatments. SD has been successfully treated with aloe vera[12] in a study involving 46 patients who received treatment with 30% aloe vera twice a day or placebo for six weeks. According to the dermatologist rating, there was a 58-percent improvement (as compared to 15% improvement in the placebo group). While patients reported 62-percent improvement (as compared to 25% to the placebo group). In addition, tea tree oil shampoo has been shown to have antifungal activity and is clinically effective in treating dandruff thought to be caused by the yeast *Pityrosporum ovale*.[16]

The herbal-based face cream used in this study forms a dense layer over the skin-injured areas and prevents oxygen supply. The resulting anaerobic conditions inhibit pathogen growth. In addition, the strong barrier properties of the cream isolate and protect the inner layers of epidermis from desiccation. Moreover, the herbal ingredients in the cream, and mostly the dipotassium glycyrrhizate (also known as licorice), offers potential anti-

**Table 4. Response of subjects when asked how they liked the product**

| EXTREMELY WELL (%) | REALLY WELL (%) | SOMEWHAT LIKED IT (%) | NEITHER LIKED NOR DISLIKED (%) | DID NOT LIKE THE PRODUCT (%) |
|---|---|---|---|---|
| 24 | 76 | 0 | 0 | 0 |

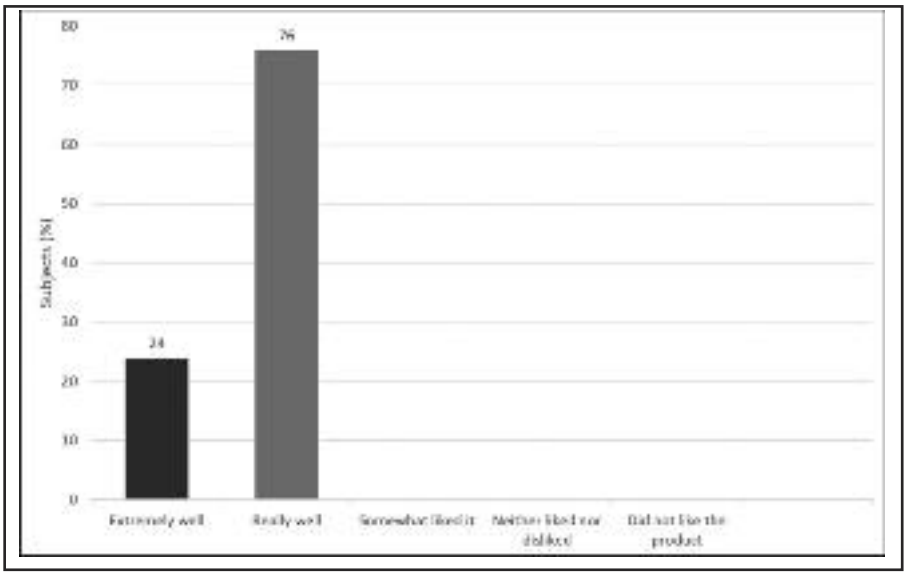



**Figure 4.** Response of subjects when asked how they liked the products

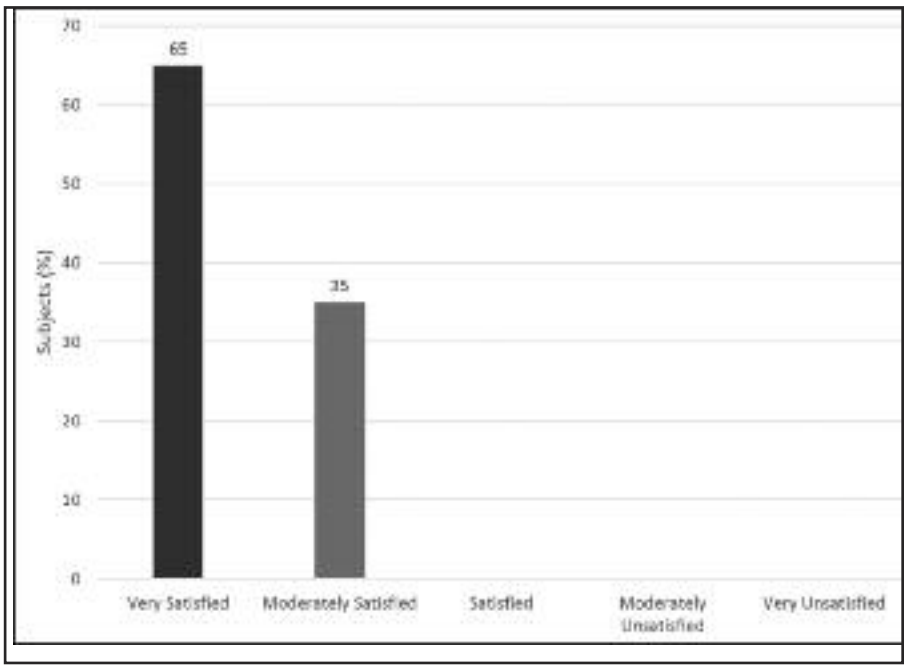



**Figure 5.** Response of subjects when asked if they were satisfied with the speed of improvement provided by the product

inflammatory,[20] antimicrobial,[21] and antifungal[22] properties, which may assist in improving and relieving the severity of the seborrheic dermatitis.

In conclusion, this six-week, interventional, open-label, safety/efficacy study demonstrated that the herbal-based face cream provided improvement for desquamation, induration, erythema, ISGA, and pruritus. Subjects were extremely satisfied with the speed of improvement, the ease of use of the face cream, and its characteristics. No safety issues were encountered.

## SUMMARY

This study was performed to determine the safety, efficacy, and ease of use of a novel herbal-based face cream in providing relief to facial seborrheic dermatitis, as measured with an ISGA using a 6-point scale and other criteria. All factors showed clinically meaningful reduction during the study with a decrease of mean scores from one visit to the next, with the exception of desquamation from Week 4 to Week 6; however, it was a major improvement from baseline.

## ACKNOWLEDGMENT

The authors thank Dr. Charles Hurwitz for assistance in drafting the article.

**Table 5. Response of subjects when asked if they were satisfied with the speed of improvement provided by the product**

| VERY SATISFIED (%) | MODERATELY SATISFIED (%) | SATISFIED (%) | MODERATELY UNSATISFIED (%) | VERY UNSATISFIED (%) |
|---|---|---|---|---|
| 65 | 35 | 0 | 0 | 0 |

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